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A scoping review: metabolomics signatures associated with animal or plant protein intake and their potential relation to cardiometabolic risk

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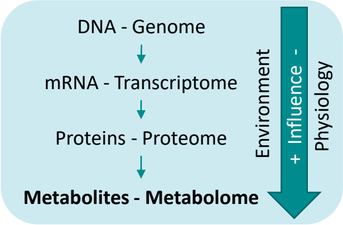
Context:

- A dietary shift from **animal protein** (**AP**) to **plant protein** (**PP**) sources have been associated with lower cardiovascular and diabetes risk
- Mechanisms are still poorly characterized and might involve many metabolic pathways.

Metabolomics is a relevant tool to explore subtle metabolic reorientations as it provides **an integrative characterization of the phenotype expressed**



Objective:

This scoping review is aimed at **gathering and analyzing the available metabolomics data associated with PP and AP-rich diets, and discussing the metabolic effects underlying these metabolomics signatures and their potential implication for cardiometabolic health**

Results:

- **24 studies selected**

Study design	Dietary comparison	n [ref]
Observational studies	AP and PP intake	1 [1]
	Omnivores vs vegetarians or vegans	6 [2-7]
	Adherence levels to defined dietary patterns	6 [8-13]
	Adherence to a posteriori (data-driven) dietary patterns	3 [14-16]
Interventional studies	Omnivores vs vegetarians or vegans	3 [17-19]
	Adherence levels to defined dietary patterns	5 [20-24]

Table 1: Classification of the studies selected

References

1: Hernández-Alonso et al, 2020, DOI: 10.1002/mnfr.202000178
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4. Wang et al, 2019, DOI: 10.1002/mnfr.201900612
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9. McCullough et al, 2019, DOI: 10.1093/ajcn/nqy385
10. Tong et al, 2020, DOI: 10.1093/jn/nxz263
11. Li et al, 2020, DOI: 10.1093/eurheartj/ehaa209
12. Walker et al, 2020, DOI: 10.3390/nu12051476
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14: O'Sullivan et al, 2011, DOI: 10.3945/ajcn.110.000950
15: Bhupathiraju et al, 2018, DOI: 10.1093/jn/nxy074
16: Wei et al, 2018, DOI: 10.1002/mnfr.201800583
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18: Rådjursöga et al, 2018, DOI: 10.3390/nu10081063
19: Djekic et al, 2020, DOI: 10.1161/JAHA.120.016518
20: Andersen et al, 2014, DOI: 10.1021/pr400964s
21: Khakimov et al, 2016, DOI: 10.1021/acs.jproteome.6b00109
22: Acar et al, 2019, DOI: 10.1002/mnfr.201800215
23. Vázquez-Fresno et al, 2015, DOI: 10.1021/pr5007894
24. Meslier et al, 2020, DOI: 10.1136/gutjnl-2019-320438

- **439 metabolites reported across studies** (mean S_M = 0.89)
  - **High heterogeneity** among the reported metabolites
  - **Metabolites related to amino acid and protein metabolism** have the highest contribution
- **46 metabolites associated to AP or PP-rich diet with a high level of evidence** (S_M > 1,51)
  - proteinogenic amino acids (30% of the 46 metabolites)
  - Biomarkers of animal products intake
  - TCA cycle intermediates
  - Very few lipids

Method:

1. Criteria for study selection

Metabolomics signatures

- Metabolomics analyses only
- Urine, plasma and serum
- Human only
- Observational and interventional studies

+

AP and PP intake

- Direct comparison of AP and PP intake
- Comparison of diets with contrasted AP and PP intake:
  - omnivores with vegetarians or vegans
  - adherence levels to defined dietary patterns (Mediterranean diet, HEI, DASH)
  - a posteriori (data-driven) dietary patterns

2. Scoring system for study contribution

Dietary contribution score S_P to account for the expected AP and PP intake differences across studies:

Type of dietary comparison	S_P
Comparison of a posteriori (data-driven) dietary patterns	0.25 (+0.125)
Comparison based on adherence to defined dietary patterns	0.5 (+0.125)
Comparison of omnivore, vegetarian and vegan diets	0.75 (+0.125)
Comparison based on AP and PP intake	1

+ 0,125 for studies providing detailed dietary data confirming intake differences in AP and PP-rich foods across groups

+

Study design contribution score S_D to account for the difference in evidence level providing by the study design:

Study design	S_D
Mechanistically based reasoning	0.2
Case-control studies	0.4
Non-randomized controlled cohort	0.6
Randomized trials	0.8
Systematic review of randomized trials	1

Assigning an overall contribution score S_C to each study included : $S_C = (S_P + S_D) / 2$

3. Metabolite selection

- Compilation of all metabolites reported as discriminant between groups in each study and cross-analysis between studies
- Attribution of a **metabolite score S_M to each metabolite reported**:

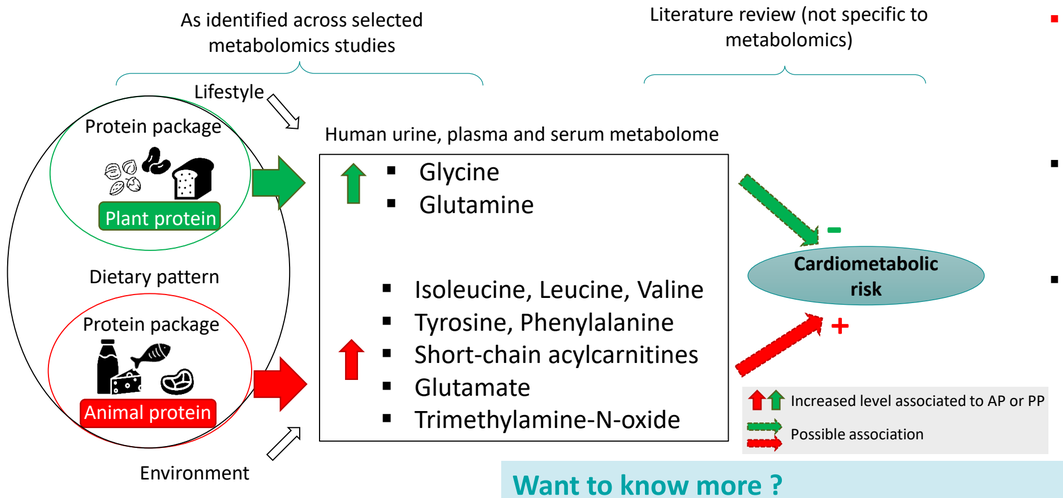
$$S_M(\text{metabolite A}) = \sum S_C \text{ (studies reporting metabolite A)}$$

- Selection of the metabolites with the highest S_M

4. Metabolite review

Literature review on the links between the selected metabolites and cardiometabolic risk

Discussion: Main metabolites discriminant between AP and PP-rich diets and their potential implication in cardiometabolic risk



Conclusions:

- **AP** and **PP**-rich diets are associated with distinct metabolites which are plausible candidates to explain some of the differential associations between diet type and cardiometabolic risk
- Very little data is available regarding the metabolomics signatures specifically associated to **AP** and **PP** intake
- More studies with a specific focus on protein type, detailed dietary data and tight intake control (see poster **P28-011-21**) are needed to better characterize the metabolomics signatures associated to **AP** and **PP** intake

Want to know more ?

Article in press for publication in *Advances in Nutrition* : Lépine et al, A scoping review: metabolomics signatures associated with animal and plant protein intake and their potential relation to cardiometabolic risk